AD-A161 629 PROPERTIES OF MATERIALS USING ACOUSTIC WAVES(U) YALE UNIV NEW HAVEN CT DEPT OF MECHANICAL ENGINEERING R E APFEL OCT 85 N00014-85-K-0215 1/1

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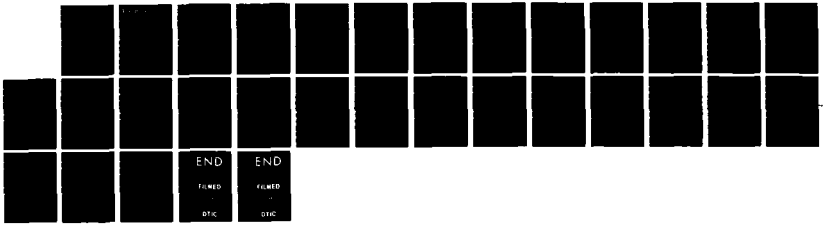
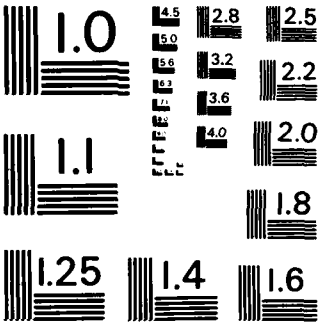




YALE UNIVERSITY

MECHANICAL ENGINEERING

(12)

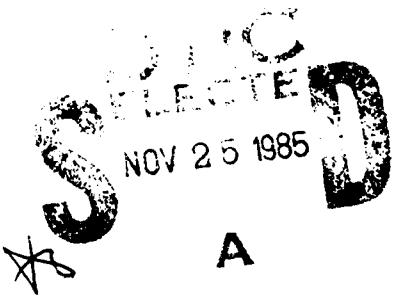
1985 Annual Report

PROPERTIES OF MATERIALS USING ACOUSTIC WAVES

N00014-85-K0215

P.I. - R.E. Apfel

October 1985



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Unclassified

SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

REPORT DOCUMENTATION PAGE		READ INSTRUCTIONS BEFORE COMPLETING FORM
1. REPORT NUMBER	2. GOVT ACCESSION NO. AD-A161629	3. RECIPIENT'S CATALOG NUMBER
4. TITLE (and Subtitle) PROPERTIES OF MATERIALS USING ACOUSTIC WAVES		5. TYPE OF REPORT & PERIOD COVERED Annual Nov. 1, 1984-Oct. 31, 1985
		6. PERFORMING ORG. REPORT NUMBER
7. AUTHOR(s) R. E. Apfel		8. CONTRACT OR GRANT NUMBER(s) N00014-85-K-0215
9. PERFORMING ORGANIZATION NAME AND ADDRESS Dept. of Mechanical Engineering, Yale University P.O. Box 2159, 9 Hillhouse Avenue, New Haven, CT 06520		10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS 61153N (Prog. El #) RR011-08-01(Proj.Task Area#) NR 384-701 (Work Unit #)
11. CONTROLLING OFFICE NAME AND ADDRESS Office of Naval Research Physics Division Office (Code 412) Arlington, VA 22217		12. REPORT DATE October 1984
		13. NUMBER OF PAGES 26
14. MONITORING AGENCY NAME & ADDRESS(if different from Controlling Office)		15. SECURITY CLASS. (of this report) Unclassified
		15a. DECLASSIFICATION/DOWNGRADING SCHEDULE

16. DISTRIBUTION STATEMENT (of this Report)

Approved for public release; distribution unlimited.

17. DISTRIBUTION STATEMENT (of the abstract entered in Block 20, if different from Report)

18. SUPPLEMENTARY NOTES

19. KEY WORDS (Continue on reverse side if necessary and identify by block number)

nonlinear parameter, radiation pressure, cavitation, levitation

20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

Our goal of characterizing materials using acoustic waves was forwarded through a number of projects: 1) We have derived a theory, and tested it on tissues, for predicting the composition of composite materials using mixture rules, such as the one we derived for the nonlinear parameter two years ago; 2) We have published one article and another is in review on our use of modulated acoustic radiation pressure on levitated drops to characterize interfaces with and without surfactants. We have begun to study in a systemmatic way the nonlinear dynamics of drops, including drop fission; 3) We have improved

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S/N 0102-LF-014-6601

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20. apparatus for 30 MHz ultrasonic scattering from microparticles (~micron size), which should allow us to discriminate between different microparticles in a liquid; 4) We have begun to study the nonlinear mechanics of hydrodynamic solitons in cylindrical (2-d) geometry; and 5) We have been studying the use of acoustic levitation for transducer calibration.

A-1

INTRODUCTION

Reported here are four areas in which we have made significant progress in the past year (1 November 1984-31 October 1985).

1. TISSUE COMPOSITION DETERMINATION USING ULTRASONIC MEASUREMENTS AND MIXTURE RULES.

This work is appended to this progress report. It should be noted that the approach discussed is not restricted to tissues. We shall consider other compositions (e.g., composite rubbers) in the near future.

2. MICROPARTICLE CHARACTERIZATION USING ACOUSTIC SCATTERING.

Mr. Roy, Prof. Apfel

The "microparticle characterization" project involves the development of an acoustic scattering technique for determining the mechanical properties of small ($\tilde{=}5$ μm) particles. We scatter tone bursts of 30 MHz center frequency and 2 μsec duration off of individual particles (e.g., biological cells) as they pass through the focal region of two confocally positioned acoustic transducers. The scattered echos are detected at 90° and 180°. With this information we employ Rayleigh scattering theory to calculate the compressibility and density of the individual particles, provided we have some a priori knowledge of the scatterer size.

Instrument development is progressing smoothly. The transducer positioning system and the flow system (for convecting the particles) are up and running. The transmit/receive switch, which permits us to detect backscattered information using the same transducer that generates the initial tone burst, is finally operational. We have also developed

and debugged the necessary instrumentation and software for demodulating the received signals, sampling the peak signal amplitude, digitizing the results, and storing the data in the computer.

At this point, the data analysis is carried out by the computer. We seek to develop a scheme for "real time" data analysis employing analog circuits. This will provide instantaneous particle information which may be used to trigger some type of downstream activity (such as sorting). We also hope to incorporate a Coulter orifice downstream of the confocal region. This device would provide size information for individual particles, thereby increasing the accuracy of the scattering calculations. We can calibrate the system by using "reference particles" such as polystryene spheres or liquid drops and we plan to run experiments with biological particles such as white blood cells.

3. INTERFACE CHARACTERIZATION USING MODULATED RADIATION PRESSURE ON ACOUSTICALLY LEVITATED DROPS.

We had to make changes in the design of our levitation cell so that surfactants could be cleaned out readily. (They tend to hide in cracks and crevices.) First we changed the original lucite cell to a rectangular glass cell (51 * 51 * 150mm, made by Vitro Dynamics, Inc.) with a hollow tube transducer (1.5 * 1.5inch) glued on the bottom of the cell by Torr seal. The major advantages of the new system are that it is very easy to clean even though there are surfactants in it, and it allows us to study the large amplitude oscillations without worrying about cavitation or the dissolving of the silver paint on the transducer.

The new system is also very efficient. It required 3 to 4 volts to levitate a hexane drop (density 0.66 g/cm^3) in water with the old system, but it only requires 2 volts using the new system.

We now have begun to study the large amplitude oxcillations using the new cell. The dynamics of the vibrating system becomes nonlinear when the amplitude of the oscillation gets sufficiently large. Different modes of oscillations are coupled together causing the shift of the resonance frequency. And the drop behaves essentially as a soft spring due to the intrinsic nonlinearity of the governing equations of motion and the boundary conditions; i.e., the resonance frequency decreases as the amplitude increases. Thus far, the system has been investigated qualitatively, because of difficulties we have encountered during the experiments. In order to study the system quantitatively, we need to be able to measure three major parameters: the amplitude of the oscillation, the pressure amplitude of the sound field, and the resonance frequency. The resonance frequency can be measured without any problem, in the same way as for the small amplitude oscillation. To measure the amplitude of the oscillation, the drop should be in a fixed position, but that has not been the case. The drop tends to move around as the amplitude increases. Furthermore, one can no longer use the voltage across the transducer as an indicator of the intensity of the sound field, because the response of the transducer may not be linear for large working voltages. Hence a calibrated transducer is needed to probe the sound field directly.

If the amplitude of the oscillation is increased further, the drop will fission. This can be achieved very easily by adding surfactants to

reduce the surface tension. We have observed drop fission for a transducer voltage of 15 volts, or so. As expected for the quadrupole mode, drop fission results in two drops of equal size.

4. NONPROPAGATING HYDRODYNAMIC SOLITON.

E. Carr Everbach, Prof. R. E. Apfel

The properties of a nonpropagating hydrodynamic soliton (as originally investigated by Wu and Rudnick) have been investigated experimentally for certain resonator geometries. In particular, solitons in annular resonators of constant width (7.5 cm) but different radii of curvature have profiles which deviate progressively from the hyperbolic secant function as the mean radius of the annulus is decreased. This distortion reaches a limit when the circumference of the inner wall becomes on the order of the soliton width, and the soliton appears to separate into two component oscillations on either side of the inner wall. These oscillations have nearly secant profiles and demonstrate most of the characteristics observed for solitons in rectangular resonators. When the radius of the inner wall is decreased further, the two component oscillations retain their relative separation distance regardless of the inner wall radius, and form two secant-profile bumps when no inner wall is present. In this case, the annular resonator becomes a circular tank, but it is surprising that the oscillations do not correspond to any of the normal modes of the tank and, in fact, occur at a drive frequency slightly below that of the lowest normal mode.

Recent efforts have been devoted to trying to understand this sub-(0.2) mode, and to determine its relationship to the nonpropagating soliton.

Theoretical analyses of both the soliton and the normal modes of the circular tank have been attempted, but due to the high nonlinearity inherent in the phenomenon, this has proved difficult. Several individuals have made very helpful suggestions in this regard, however, and further experimental work is being carried out to shed light on the problem.

Despite the experimental and theoretical difficulties, the non-propagating hydrodynamic soliton is well enough understood to be able to apply it to other nonlinear wave systems. Future work in this area might focus on the feasibility of an analogous acoustic, light, or flexture soliton. Preliminary work in this area has begun and may be developed further.

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Accepted for publication, J. Acoust. Soc. Am.

Prediction of Tissue Composition from Ultrasonic Measurements and Mixture Rules

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Abstract

A methodology is presented for predicting the composition of tissues from measurements of the density, sound velocity, and acoustic nonlinear parameter, using mixture laws for the density, compressibility, and nonlinear parameter. It is shown that the mixture law for the nonlinear parameter plays an essential part in this methodology, which leads to the prediction of the volume fractions of water, protein, and fat in a given tissue. Data from the literature for solutions, blood, normal tissue, and cancerous tissue are investigated, and predicted fractions are consistent with tissue compositional information available in handbooks. More experimental work is needed with tissues of known composition in order to more fully test the proposed methodology.

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Introduction

To what extent can simple mixture models allow for the prediction of the composition of tissues? For instance, simple mixture models for the density, ρ, and compressibility, β, can be written as[1]

$$\rho = \sum_{i}^{n} \rho_i x_i \qquad 1$$

$$\beta = \sum_{i}^{n} \beta_i x_i \qquad 2$$

where the x_i are the corresponding *volume fractions* and n is the number of different components that are sufficient to describe the material. In our tissue work we will consider three basic components: i = 1 is an isotonic water solution, i = 2 is "pure" protein (see below), and i = 3 is pure fat (e.g. lipid or oil base). To illustrate the utility of equations 1 and 2, we consider the work of Weiser[2] and Weiser and Apfel[3] who measured density and compressibility of red blood cells (RBC's) in different saline solutions, ranging from hypotonic (74 mM NaCl, 20 mM Tris) to hypertonic (320 mM NaCl, 20 mM Tis). RBC's can be modeled as a mixture of salt water and protein (i.e. no fat). As figure 1 illustrates, the linear mixture model works quite well. Moreover, the extrapolation of this data to 100% protein gives us values of the effective density and compressibility of pure protein as $\rho_2 = 1.37$ g/cm^3 and $\beta_2 = 0.94\times10^{-11}$ cm^2/dyne. Note, also, that it appears that the predicted sound velocity, c_2, of the mixture, given in terms of ρ_2 and β_2 by $c_2 = 1/(\rho_2\beta_2)^{\frac{1}{2}}$, does not follow a linear mixture model; more data points, however, are necessary to validate this contention.

Does this kind of mixture modeling work for the nonlinear parameter, B/A, of the solution? Here B/A is defined by

$$\frac{B}{A} = 2\rho c \left(\frac{dc}{dP}\right)_s = \left[\frac{d(1/\beta)}{dP}\right]_s - 1 \qquad 3$$

where $(dc/dP)_s$ gives the change in sound velocity for an adiabatic pressure change,[4] and $d(1/\beta)/dP$ represents the material's "stiffness" change with pressure.

Apfel recently derived an effective nonlinear parameter of a mixture as[5]

$$(B/A) = \frac{1}{\beta^2} \sum_{i=1}^{n} \beta_i^2 \left(\frac{B}{A}\right)_i x_i. \qquad 4$$

Because of β's dependence on the volume fractions, we see that Eq.4 is not linear in the x_i's.

Equations 1, 2, and 4 plus the condition that $x_1 + x_2 + x_3 = 1$ constitute the four equations to be solved. Assuming that the tissue properties ρ, β, and B/A are measured, we have four equations and three unknowns — the volume fractions of the aqueous medium (water or saline solution), protein, and fat. How does one solve for the optimal choice of the x_i?

Statement of the Mathematical Problem

First we repeat equations 1, 2, and 4 in matrix format, $AX = B$, assuming the equations to be exactly true and considering three components in the mixture,

$$\begin{bmatrix} \rho_1 & \rho_2 & \rho_3 \\ \beta_1 & \beta_2 & \beta_3 \\ \beta_1^2(B/A)_1 & \beta_2^2(B/A)_2 & \beta_3^2(B/A)_3 \end{bmatrix} \begin{bmatrix} x_1 \\ x_2 \\ x_3 \end{bmatrix} = \begin{bmatrix} \rho \\ \beta \\ \beta^2(B/A) \end{bmatrix}. \qquad 6$$

Later we will find it convenient to normalize each of the equations in Eqs.6 by their right hand sides, so that B is a vector of ones. The equations in this matrix are subject to the constraint:

$$x_1 + x_2 + x_3 = 1. \qquad 7$$

But the equations represented by the matrix are only approximations. In Eq.6, the B vector components are based on measured values of ρ, β, and B/A. When a set of x's are chosen, these will produce effective properties, indicated by primes, that differ from the measured values by Δ_i; we define the Δ's as the normalized quantities, as follows:

$$\Delta_1 \equiv (\rho'-\rho)/\rho \qquad 8$$

$$\Delta_2 \equiv (\beta'-\beta)/\beta$$

$$\Delta_3 \equiv [(B/A)' - (B/A)]/(B/A)$$

Our goal is to find x_1, x_2, x_3 such that these errors are minimized. We choose the criterion that we minimize Q, where

$$Q \equiv (\Delta_1^2 + \Delta_2^2 + \Delta_3^2). \qquad 9$$

We do this by the method of the Lagrange multipier. The details, given in Appendix A, result in a set of four equations and four unknowns.

Input Parameters

The simultaneous solution of the four algebraic equations of Eqs. A-5 depends on the input parameters, the elements in the matrix A, and the measured tissue or solution properties, the elements in the B vector. Table 1 gives the input parameters used, where T is the temperature in ^{o}C.

The temperature dependence of water's properties are taken from handbooks and, for (B/A), from the work of Coppens, et al.[6] Protein, considered to be semi-solid, is assumed to have a negligible temperature dependence for density and compressibility over the 15 celsius degree span that encompasses all the data to be presented. The temperature dependences of the properties of fat follow those of many oils.[7,8] Namely, approximately -0.001 g/cm^3/^{o}C for the density and about -3.5 meters/s/^{o}C for the velocity of sound, from which the compressibility can be calculated ($\beta = 1/\rho c^2$). The sound velocity for pure fat at 20^{o} is taken as 1451 m/s. (At 37^{o}C it is estimated at 1391.5 m/s.)

Note that we must assign, somewhat arbitrarily, a value for the nonlinear parameter of pure protein. This is true because the weighting factor, β_2^2, in Eq.4 is on the order of 1/20 of β_1^2, so that the value of B/A for the solution or tissue is rather insensitive to the choice of $(B/A)_2$. We choose a value of 10 (at 20^{o}C) since many carbon based compounds have B/A values between 9 and 11.

For "pure" fat, the nonlinear parameter is assigned to be 11 at 20^{o}C, taking guidance from our earlier work in which the nonlinear parameter of pure castor oil was measured at 12.0.[3] The temperature dependence of B/A fat is taken to be +.03/^{o}C, similar to that for glycerol.[9] Our

sensitivity analysis in Appendix B gives estimates of the effects of changes in our input parameters on our predicted volume fractions.

Results for Aqueous Solutions

We now consider the results based on available input data from the literature.[9,10,11] The results for solutions are given in Table 2.

For dextrose and dextran solutions we substitute for protein, sugar with "pure" density and compressibility given by $\rho_2 = 1.53$ g/cm^3 and $\beta_2 = 0.5\times10^{-11}$ cm^2/dyne, as determined from Eqs.1 and 2 using density and sound velocity data reported in the literature. $(B/A)_2$ is taken as 10 because the atomic make-up of proteins and sugars is similar in many respects. (See, also, Appendix B for a sensitivity analysis.)

To convert the concentration, α, in grams/cm^3 to volume fraction, we first convert α to mass fraction, m,

$$m = \alpha/\rho, \text{ in grams/100 grams solution}$$

and, then using Eq.1, the defining relation for a mixture involving protein (or sugar) and water, we get

$$x_2 \text{ (protein or sugar volume fraction)} = \frac{1}{1 + \left(\frac{1-m}{m}\right)\frac{\rho_2}{\rho_1}} \qquad 10a$$

$$x_1 \text{ (water volume fraction)} = \frac{1}{1 + \left(\frac{m}{1-m}\right)\frac{\rho_1}{\rho_2}} \qquad 10b$$

The calculated volume fractions, and those deduced from the given concentrations, are expected to agree reasonably well, since ρ_2 and β_2

are deduced from the data. What is perhaps worthy of note, however, is that the calculated volume fraction of fat is negligibly small, as expected, and that the measured value of B/A is, indeed, significant in the calculation. That is, if B/A were 7.04 instead of 6.04 for dextrose at 30° (α = 28.9 g/cm³), the volume fraction of water and protein would each change away from the correct value by about 8%. Therefore, B/A results are seen as part of a consistent set of data which determines accurate compositional information.

Also of note are some negative volume fractions, always of small magnitude. These occur occasionally because the criterion we choose for the optimal x_i (Eq.9) does not constrain the x_i to be positive.

Results for Tissues

Table 3 presents results for the components (x_1, x_2, x_3) of tissues for which data on density, sound velocity, and B/A data are available. Because of the sensitivity of the results to the accuracy of B/A measurements (see Appendix B), we accept only B/A data having error bars of less than ±5%. This rules out all solid tissue B/A data employing the finite element method.

There are a number of consistencies in the results that support our confidence in our methodology. First, if one looks at the data for multiple myeloma,' we see changes of 10% in the B/A data, for a change of 15°C, whereas the corresponding predicted change in the volume fraction of the predominent component, water, is only about 1%. Since the same sample was used over the entire temperature range, and since the density change is less than 1% over a 15° temperature change, we expect the

volume fractions to remain the same.

Second, the breast fat data correctly predicts minimal amounts of protein, and therefore, like the sugar solutions data which predicted negligible fat, conforms to reality. One anomaly does exist in the measured data, namely, the sharp change in the temperature dependences of the sound velocity[12] and nonlinear parameter.[9] Nevertheless, the predicted tissue composition shows reasonable consistency with temperature.

Finally, the true test of our approach is whether the predicted compositions correspond quantitatively to reality. Analyses of tissue composition are reported in the literature and summarized in handbooks. Usually ranges are given, because the compositions depend on a number of factors, such as age, diet, state of hydration, etc. Nevertheless we are able to make some comparisons. For instance the *mass* fractions of water and protein for human liver from the Handbook of Biological Data[13] are 0.73-0.77 and 0.18, respectively, with an estimate for fat from animal data being 0.03-0.06. Our corresponding results (corrected to mass fractions) are 0.76, 0.20, .04. (The protein fraction is expected to be higher, because it includes other dissolved components that tend to reduce the compressibility.)

For cancerous tissue it is generally recognized that the water fraction increases. For instance, in rat hepatoma the water fraction is about 0.71 for normal liver and 0.82 for the hepatoma, whereas the fat total is .062 for normal liver and 0.032 for the hepatoma (protein data was not given).[14] From the data[3] we have analyzed, the water fraction goes from 0.76 in normal human liver to 0.90 for multiple myeloma, about the

same percent change as for the rat data. For fat, the mass fraction for the human liver is 0.04 and for myeloma is .02. Thus the trends are confirmed qualitatively and, in some cases, quantitatively by our predictions.

General Discussion

Should the mixture rules be valid? Or are there substantial errors in each of them that are in some way compensated for when the rules are taken as a set? We suggest that this question depends on the degree to which molecules of the individual components (water, protein, or fat) intermix as compared to "sticking to their own kind." That is, what fraction of water molecules are surrounded by other water molecules and what fraction of them are in contact with fat or protein?

If the intermixing is substantial, as with a 20% mixture of methanol in water, then the mixture rule is invalid. (The value of B/A for methanol-water solution actually has a minimum which cannot be predicted by our mixture model.[3]) But if large numbers of the same atom groups are in close proximity, as with protein or fat, which have high molecular weights, then the mixture rule is likely to be valid.

As Hartmann[15] and others have discussed, the nonlinear parameter is tied to the shape of the intermolecular or interatomic potential (molecular scale). Thus, structures such as the aggregates of biological cells that make up tissue, which are much larger than the intermolecular scale, should not play a significant role in determining B/A, and, therefore, B/A should not provide information about the hierarchal structures of tissue. Rather, by providing an additional independent quantity, related to the pressure dependence of the material's stiffness, one is able to characterize more fully the composition

of complex materials, such as tissues.

If spatially dependent B/A measurements can be performed *in vivo*, as with sound velocity measurements,[12] then significant opportunities exist for diagnosing pathological conditions in soft tissues. Although there have been reports of such in vivo measurements,[15] a statement, made in the description of the work, namely that B/A is small for fat, is totally inconsistent with *in vitro* measurements, suggesting that the nonlinear parameter was not isolated from other factors.

Further work is needed in accurate measurements of biological systems for which the compositions are well known and, therefore, for which comparisons with our composition determination methodology are possible.

Acknowledgment

I thank B.-T. Chu of Yale for his suggestion of the mathematical approach followed in this paper and Leon Frizzell of the Bioacoustics Research Laboratory, University of Illinois, for providing a copy of reference 11 prior to its publication. This work is supported, in part, by the U.S. Office of Naval Research.

Appendix A Mathematical Analysis

We begin our analysis by putting Eq.4 in a vector and indexed format

$$Q = \tilde{\Delta} \cdot \Delta \qquad \text{A-1}$$

$$= (A_{ij}x_j - B_i)(A_{ik}x_k - B_i) - \lambda(x_1 + x_2 + x_3 - 1).$$

where Δ is the column matrix having Δ_1, Δ_2, Δ_3 as its components, and $\tilde{\Delta}$ is the transpose of Δ. Here the A's and B's represent the elements in the normalized form of Eq.6 (see Table 1). In the format of Eq. A-1 the double subscript implies summation over the repeated indice, and λ is the Lagrange multiplier.[17]

The minimization procedure is performed through

$$\frac{\partial Q}{\partial x_1} = 0, \frac{\partial Q}{\partial x_2} = 0, \frac{\partial Q}{\partial x_3} = 0 \qquad \text{A-2}$$

or

$$\frac{\partial Q}{\partial x_n} = A_{ij}\delta_{jn}(A_{ik}x_k - B_i)+(A_{ij}x_j - B_i)A_{ik}\delta_{kn} - \lambda = 0 \qquad \text{A-3}$$

where $\delta_{jn} = \frac{\partial x_j}{\partial x_n}$ is the Kronecker delta.

Combining terms gives:

$$\frac{\partial Q}{\partial x_n} = A_{in}(A_{ik}x_k - B_i)+(A_{ij}x_j - B_i)A_{in} - \lambda = 0 \qquad \text{A-4}$$

$$= 2A_{in}(A_{ik}x_k - B_i) - \lambda = 0$$

Including the summation explicitly gives the four equations:

$$2 \sum_{i=1}^{3} A_{i1}(A_{i1}x_1 + A_{i2}x_2 + A_{i3}x_3 - B_i) - \lambda = 0$$

$$2 \sum_{i=1}^{3} A_{i2}(A_{i1}x_1 + A_{i2}x_2 + A_{i3}x_3 - B_i) - \lambda = 0 \qquad \text{A-5}$$

$$2 \sum_{i=1}^{3} A_{i3}(A_{i1}x_1 + A_{i2}x_2 + A_{i3}x_3 - B_i) - \lambda = 0$$

$$x_1 + x_2 + x_3 + (0)\lambda = 1$$

These four equations can be solved analytically or numerically (see Appendix B) for the four unknowns, x_1, x_2, x_3, λ, and the Δ's can be calculated from Eqs. 8.

Appendix B — Accuracy and Sensitivity Checks

A number of checks were performed to test the accuracy and reasonableness of our formulation:

1) Accuracy of the inversion algorithm

When tested with simulated data, the algorithm reproduced the correct results within 2 parts in 10,000.

2) Importance of B/A relationship

If we solve Eq.1 and 2 with the constraint equation, $x_1 + x_2 + x_3 = 1$, for the case of breast fat at 30°C, we get $x_1 = -0.096$, $x_2 = 0.159$, $x_3 = 0.937$, as compared to the results in Table 3 of $x_1 = 0.418$, $x_3 = .006$, and $x_3 = .577$ when the nonlinear parameter equation is included. This result points to the necessity of using the full complement of information available in order to achieve reasonable results.

3) Effect of input data

If one or more of the input parameters is close to the measured values of ρ, β, or B/A for the solution or tissue, then the results may become especially sensitive to the input parameter. For instance, if β_3 is reduced by 5%, the results for breast fat at 22°C change as follows: water fraction reduced by 19%, fat fraction up 16%, and a significant change in the protein fraction. Similar changes occur for measured B/A values that approach the value of B/A for pure fat (~11). The effect is smaller for tissues for which the B/A value is lower, as with most other tissues (e.g. liver). But the effect is not negligible. For instance, if we take the liver data and reduce the measured density by

10%, the predicted water, protein, and fat volume fractions change by 0.8%, 2.9%, and 3.5% respectively. The corresponding changes for a 10% increase in B/A are 7.5%, 10.6%, and over 100%.

This sensitivity check reinforces our caveat that accurate measurements of tissue properties, such as are possible with phase methods for B/A[9,13,18], are a prerequisite for getting reliable compositional information. Moreover, we should measure B/A of lipid oils in order to get a more accurate estimate of the nonlinear parameter of pure fat, thereby reducing our uncertainties in tissue composition especially for those tissues containing a significant fat component.

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Figure Caption

Figure 1 Plot of density, compressibility, and deduced sound velocity of red blood cells as a function of the volume fraction of protein. (from reference 2)

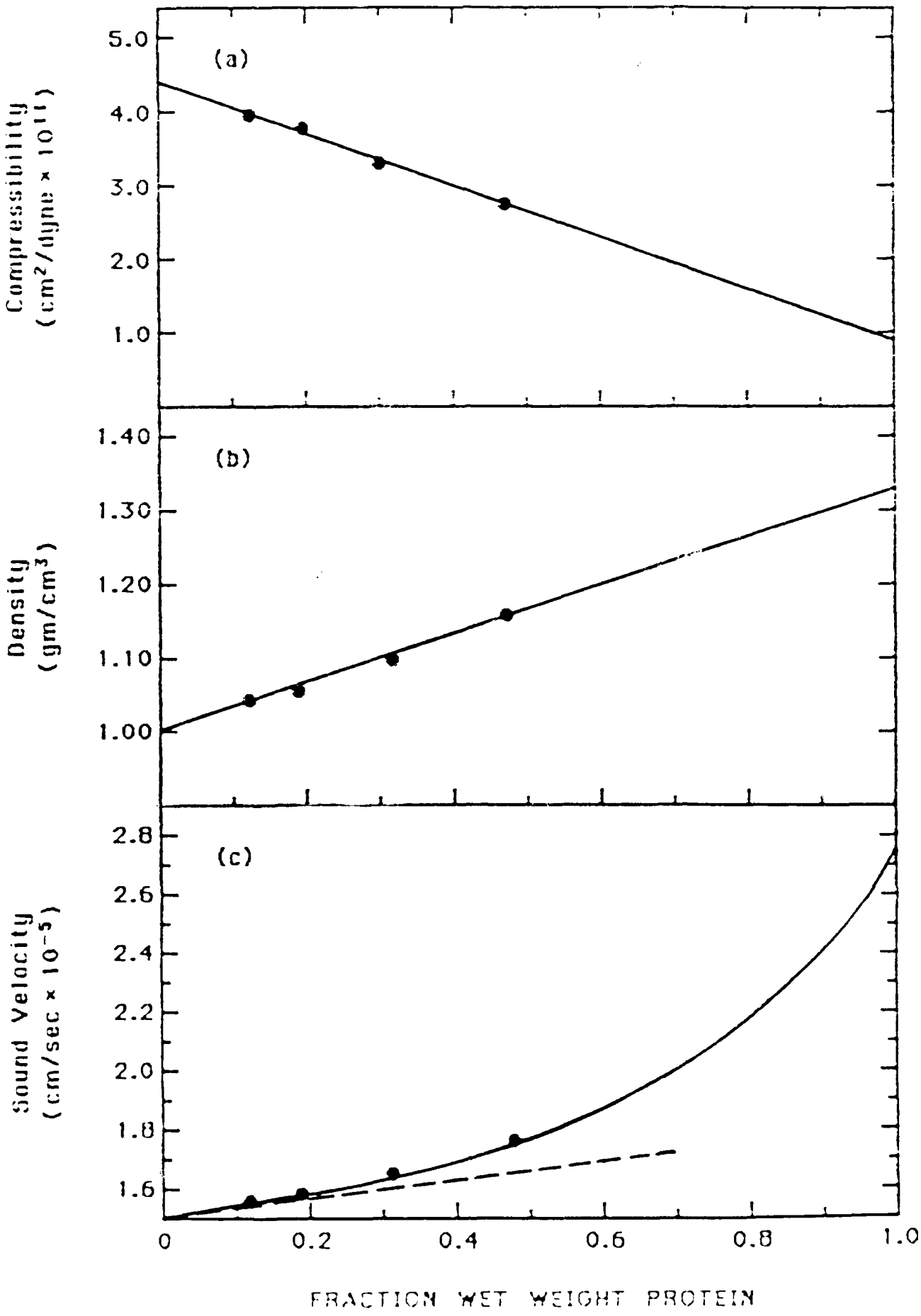
(a)
Compressibility
(cm²/dyne × 10¹¹)
5.0
4.0
3.0
2.0
1.0
(b)
Density
(gm/cm³)
1.40
1.30
1.20
1.10
1.00
(c)
Sound Velocity
(cm/sec × 10⁻⁵)
2.8
2.6
2.4
2.2
2.0
1.8
1.6
0
0.2
0.4
0.6
0.8
1.0
FRACTION WET WEIGHT PROTEIN

TABLE 1 - INPUT PARAMETERS

$$\rho A_{11} = \rho_1 = \begin{cases} 1.005 - .00029\times(T-20) & \text{for tissues and whole blood} \\ .998 - .00029\times(T-20) & \text{for dextrose, dextran, and BSA solution} \end{cases}$$

$$\rho A_{12} = \rho_2 = \begin{cases} 1.37 & \text{for "pure" protein} \\ 1.53 & \text{for "pure" sugar (for dextrose and dexttran solutions)} \end{cases}$$

$$\rho A_{13} = \rho_3 = 0.88 - 0.001\times(T-20)$$

$$\beta A_{21} = \beta_1 = 1(\rho_1 c_1^2), \text{ where } c_1 = \begin{cases} 1.519\times10^5 + 240\times(T-30); & \text{saline} \\ 1.510\times10^5 + 240\times(T-30); & \text{sugar} \end{cases}$$

$$\beta A_{22} = \beta_2 = \begin{cases} 0.94 & \text{for pure protein}^{*} \\ 0.5 & \text{for pure sugar (for dextrose and dextran solutions)}^{**} \end{cases}$$

$$\beta A_{23} = \beta_3 = 5.4(1 + .00463\times(T-20)), \text{ where } c_3 = 1.451\times10^5 \text{ at } 20^{\circ}C$$

$$\beta^2(B/A)A_{31} = \beta_1^2(B/A)_1, \text{ where } (B/A)_1 = 5.3 + 0.02\times(T-30)$$

$$\beta^2(B/A)A_{32} = \beta_2^2(B/A)_2, \text{ where } (B/A)_2 = 10.0 + .031\times(T-20) \text{ for protein and sugar}$$

$$\beta^2(B/A)A_{33} = \beta_3^2(B/A)_3, \text{ where } (B/A)_3 = 11.0 + 0.031\times(T-20)$$

Densities in g/cm^3; compressibilities in $cm^2/dyne\times10^{11}$; T in $^{\circ}C$; c in cm/s.

Note that all A_{ij}'s are normalized so that all B_i's are 1.

* This value is consistent with compressibilities of solid polymers, such nylon, polystyrene and lucite.

** This value follows from the compressibility of solid dextrose, as measured by Bridgman.[19]

TABLE 2 RESULTS FOR SOLUTIONS †

Solution	Temp °C	input parameters ρ	β	B/A	known sol'n parameters a	m	x_1	x_2	calc. vol. fract. x_1	x_2	x_3	discrepancies Δ_1	Δ_2	Δ_3
[illegible]	25	1.045	3.95	6.23	.20	.19	.85	.15	.811	.155	.034	-.006	.004	2e-5
[illegible]	30	1.094	3.50	6.68	.389	.356	.71	.29	.717	.267	.015	-5e-4	-1e-4	2e-6
Whole blood	30	1.056	3.84	6.3	.23 (est.)	.21	.85	.15	.815	.155	.030	-7e-4	-3e-4	3e-5
Dextrose	30	1.1	3.54	6.04	.289	.262	.81	.19	.813	.211	-.024	.01	.004	-1e-4
Dextrose	30	1.092	3.62	5.96	.25	.229	.84	.16	.831	.191	-.022	.007	.003	-1e-4
Dextran T150	30	1.088	3.74	5.94	.24	.221	.84	.16	.844	.168	-.012	.002	7e-4	2e-5
Dextran T150	30	1.088	3.74	6.05	.24	.221	.84	.16	.832	.170	-.008	-.001	-6e-4	2e-5
Dextran T2000	30	1.09	3.70	6.2	.264	.242	.83	.17	.820	.180	.000	-.001	-6e-4	-2e-5
Dextran T2000	30	1.09	3.70	6.03	.26	.239	.83	.17	.833	.177	-.010	.001	5e-4	-2e-5

† Data from ref. 11 except BSA data at 25°C, which is taken from ref. 10.

‡ BSA is Bovine Serum Albumin

TABLE 3 - RESULTS FOR TISSUE*

Material	Temp	ρ measured density g/cm^3	c measured sound velocity m/s	β inferred compressibility $= \frac{1}{\rho c^2}$ $\times 10^{-11} cm^2/dyne$	B/A measured nonlinear parameter	x_1 water (saline)	x_2 protein	x_3 fat	Δ_1	Δ_2	Δ_3
						Volume Fractions			Discrepancies		
Breast fat	22	.915	1481[12]	4.98	9.206	.452	-.009	.559	.017	.001	4e-4
	30	.913	1477[12]	5.03	9.909	.418	.006	.577	.017	.01	-2e-4
	37	.911	1436[12]	5.39	9.633	.455	-.040	.584	-.006	-.004	3e-4
Multiple myeloma	22	1.03	1537	4.11	5.603	.899	.091	.010	.006	.002	5e-5
	30	1.03	1549	4.07	5.796	.902	.082	.016	4e-6	2e-6	6e-8
	37	1.03	1556	4.05	6.178	.887	.078	.036	-6e-3	-.003	9e-5
Human liver	30	1.05	1573	3.85	6.54	.798	.157	.045	.003	.004	1.7e-5

* Data from ref. 9 unless otherwise marked

END

FILMED

1-86

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END

FILMED

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